Healios

“To be the change in an ever evolving world
through enrichment of living”

HEALIOS K.K. (TSE 4593)

FY2017 3Q Financial Results

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1. Financial Highlights

Statement of income

(Million yen)

	FY 2016 3Q	FY 2017 3Q		
			YoY change	Main reasons for increase/decrease
Sales	57	27	▲30	
Operating income	▲3,053	▲1,797	+1,255	Research & Development Cost decreased ＋1,302
Ordinary income	▲3,099	▲1,846	+1,253	-
Net income	▲3,103	▲1,209	+1,894	Gain on Business transfer +641
R&D	2,644	1,342	▲1,302	▲1,809 (Due to MultiStem License-in in FY2016)
Amortization of goodwill	75	33	▲41	-
Number of employees	53	71	+18	-

Balance sheet

(Million yen / %)

		December 31, 2016	September 30, 2017		
				Change	Main reasons for increase/decrease
	Current assets	8,073 (88.0%)	16,609 (97.6%)	+8,535	Cash and deposit ＋8,514 (Cash and deposit balance 16,341)
	Non-current assets	1,101 (12.0%)	413 (2.4%)	▲687	Goodwill ▲691
Total assets		9,174 (100.0%)	17,023 (100.0%)	+7,848	
	Current liabilities	772 (8.4%)	1,478 (8.7%)	+706	
	Non-current liabilities	2,408 (26.2%)	2,275 (13.4%)	▲132	
Total liabilities		3,180 (34.7%)	3,754 (22.1%)	+573	
Total equity		5,994 (65.3%)	13,268 (77.9%)	+7,274	Capital etc. ＋8,444 Earned surplus ▲1,209
Total assets		9,174 (100.0%)	17,023 (100.0%)	+7,848	

2. Updates in FY2017 3Q

Issuance of stock acquisition rights

Issued on March 2017, Assignee: Nomura Securities

[As of the end of October 2017]

Number of exercised shares : 5,750,000 common shares (80.5%)

Total fund raising : 8.02 billion yen

Number of unexercised latent shares : 1,395,700 common shares

* In the case of the final financing amount being less than the estimated amount, Healios will screen and make judgments on projects based on their short-term business potential and strategic importance, and will prioritize investment them accordingly.

[Purpose of the funds] Disclosed on March 2, 2017

*Total fund raising originally estimated: Approximately 13 billion yen.
(Amount could change depending on the share price trend going forward.)

Billion yen

Development for HLCM051 (Ischemic stroke in Japan)	4.63
Development for HLCR012 (iPSC-derived RPE cells for Dry AMD in US and Europe)	1.01
Development for HLCL041 (Organ bud)	0.78
License fee to introduce new seeds and development fee	4.81
Loan repayments	2.5

Pipeline

Field	Development Code	Indication	Market	Pre-clinical test	Phase I Trial	Phase II Trial	Phase III Trial	Apply-approve	On the Market	Progress Status
Somatic stem cell Regenerative Medicine	HLCM051	Ischemic Stroke	Japan	→	→	→	→			Phase 2/3 Trial
iPSC Regenerative Medicine	HLCR011	Wet AMD	Japan	→						Start of clinical studies originally scheduled in 2017 may be delayed
	HLCL041	Metabolic Liver Disease	Japan	→						Joint research with Yokohama City University
	HLCR012	Dry AMD	US	→						Technical transfer
	HLCR012	Dry AMD	EU	→						Global Trial Under Consideration based on US Phase III Trial

* Compound drug pipeline (HLM021, HLM022, HLM023): Business transfer completed on April 30, 2017

HLCM051: Clinical trial status

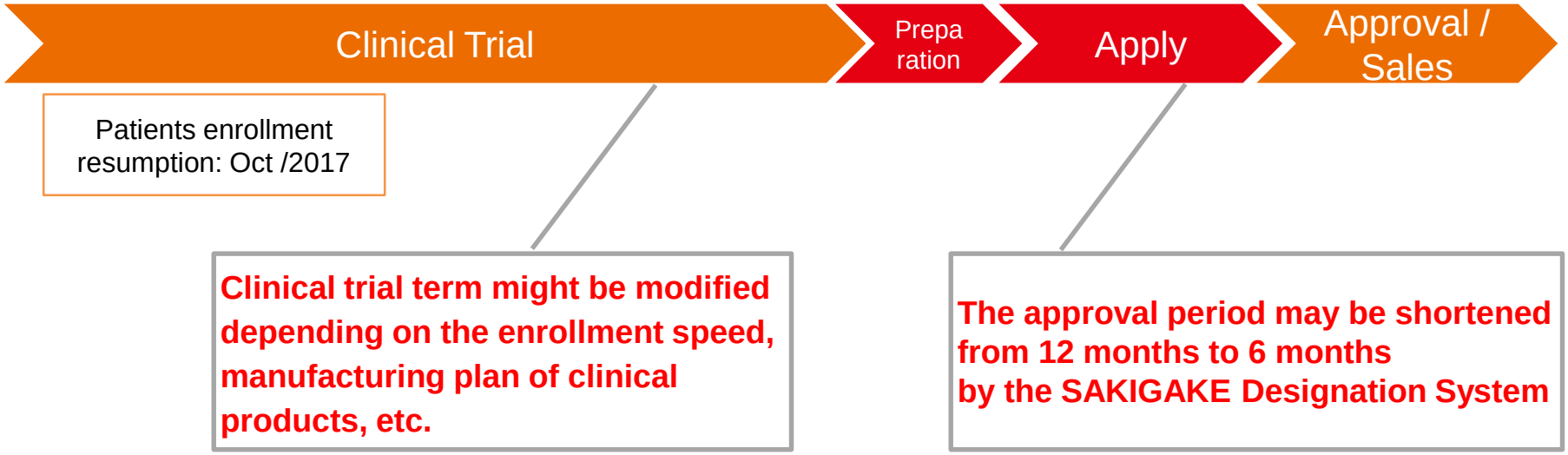
Somatic stem cell regenerative medicine

HLCM051
MultiStem®

“Placebo-Controlled, Double-Blind, Phase 2/3 Efficacy and Safety Trial of HLCM051 (MultiStem®) in Patients With Ischemic Stroke”
(**TREASURE study)**

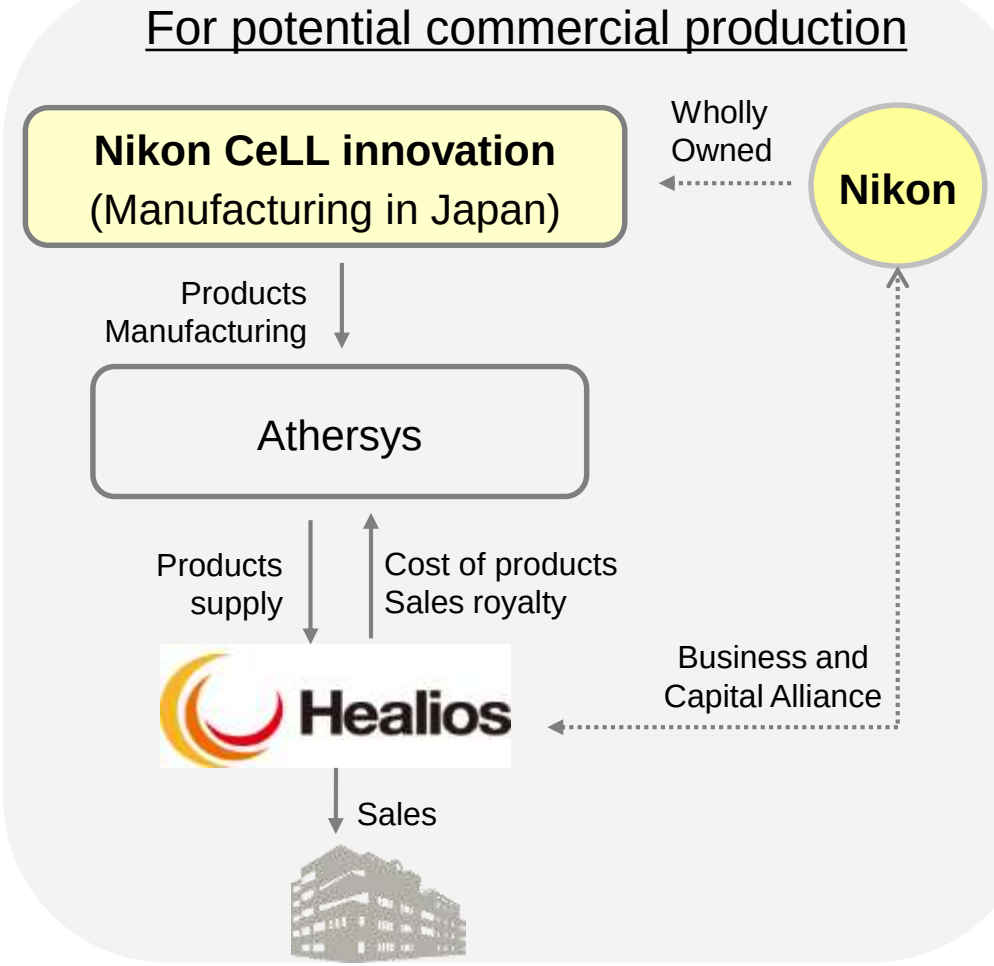
August 24, 2017: Patient enrollment temporally suspended due to a deviation in the placebo

October 25, 2017: Patient enrollment has been resumed

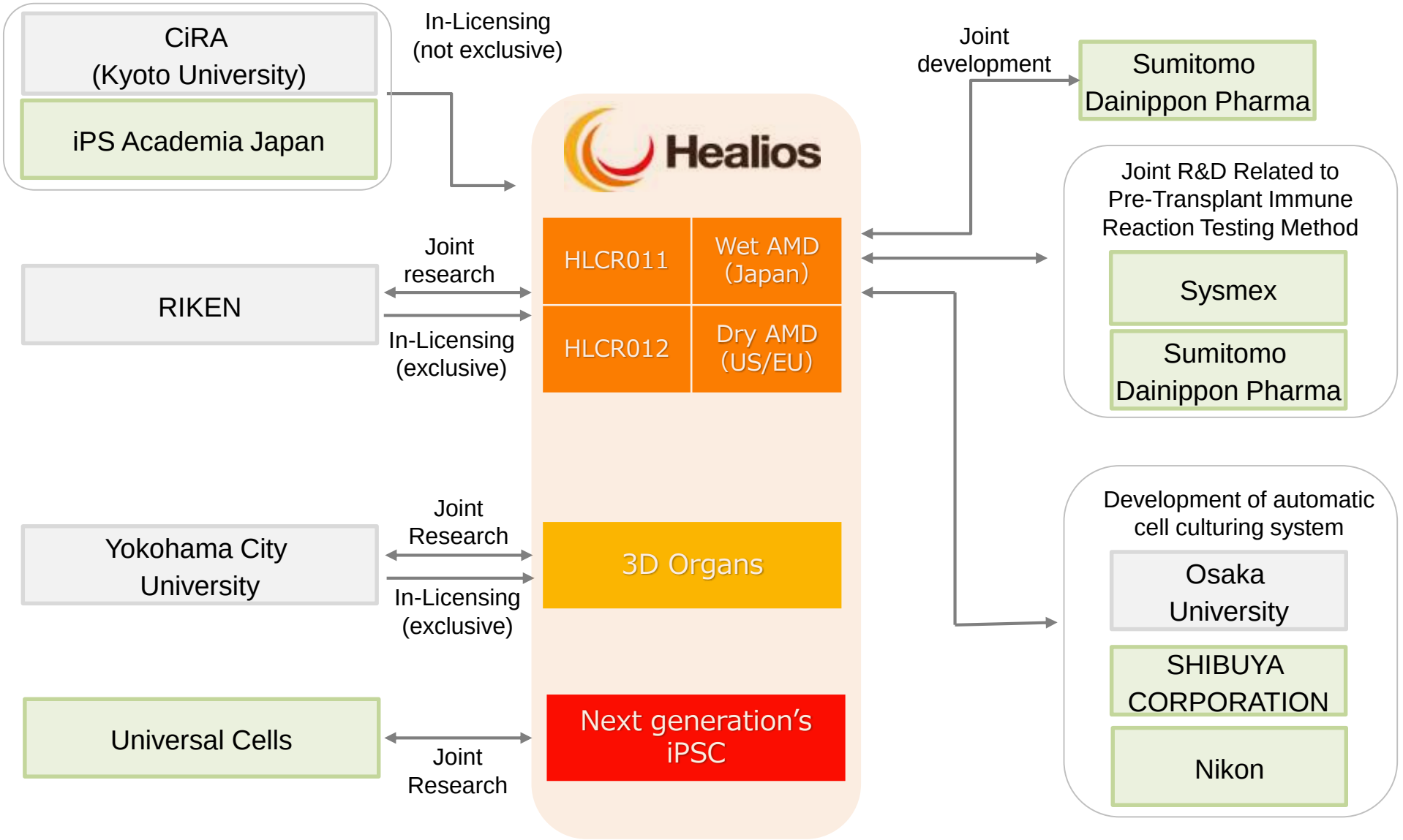


HLCM051: Business Partner

In October 2017, Nikon CeLL innovation executed a manufacturing service agreement with Athersys in preparation for the commercialization of HLCM051



iPSC Regenerative Medicine field: Business Partner



3. Details of Somatic Stem Cell Regenerative Medicine

Introduced new pipeline: HLCM051 in January 2016

Athersys inc.

（Source）Athersys

- Cell therapy product based on patented technology
- Developing for “off-the-shelf” administration: no tissue matching needed
- Long shelf life: can be kept frozen in a stable condition for years
- Consistent safety profile
- Promotes healing and tissue repair through multiple mechanisms of action
- Not a permanent transplant: cells cleared from the body over time

Outline of ischemic stroke in Japan

Ischemic stroke

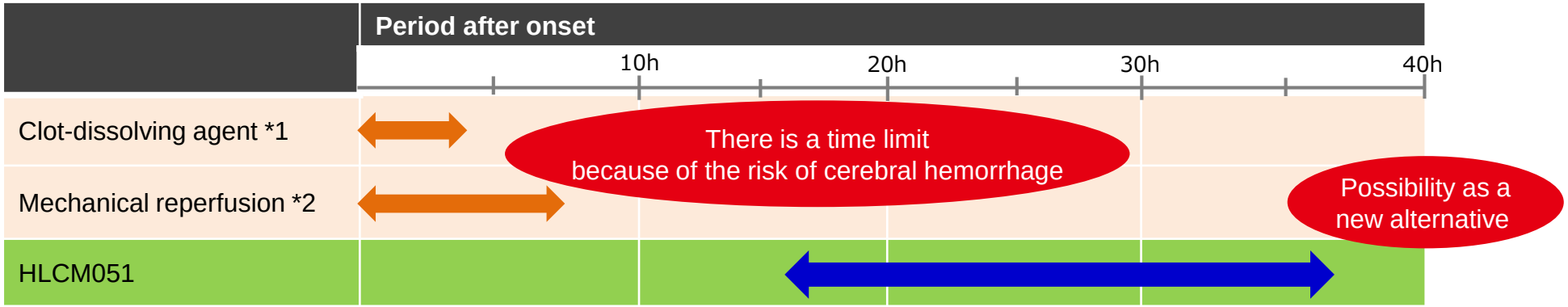
Ischemic stroke, which represents the most common form of stroke (70–75% of cases in Japan), is caused by a blockage of blood flow in the brain that cuts off the supply of oxygen and nutrients, resulting in tissue loss

It is estimated that 37.9% of bedridden patients and 21.7% of persons who were in need of care were affected by ischemic stroke

（Source）Athersys

Treatment in accordance with the period after onset

■ Expected development of a new therapy that can be applied in a longer treatment widow period following the onset of ischemic stroke (ability to help more patients)



*1: Dissolves blood clots in the brain vessels. *2: Insertion of the catheter into a blood vessel and recovery of the thrombus directly with a wire

(Note) This material was prepared to explicitly describe the major therapeutic options for ischemic stroke and their treatment window periods after onset. Appropriate treatments are conducted according to patients' conditions and classification of their symptoms. Experimental or investigational treatments not included in the above are also performed.

Annual number of new patients with ischemic stroke in Japan

Target population

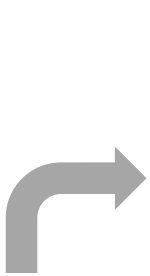
	Japan	Note
Number of patients (yearly)	**230,000 – 330,000**	Annual medical costs for ischemic stroke estimated at 1070.7 billion yen（2009）
Severe patients（atherothrombotic and cardiogenic cerebral infection)	**130,000**	
patients within 36 h after onset	**62,000**	

(Source) Healios estimated the annual number of new patients with ischemic stroke in Japan according to materials issued by the Fire and Disaster Management Agency, the Ministry of Internal Affairs and Communication, and the Ministry of Health, Labour and Welfare – DATAMONITOR epidemiological estimates also shown as upper end of range.
(Source) Healios estimated the percentage of patients who reach the hospital within 36 hours after onset at 47% according to the results of its market research.

(Note) Calculated using 2013 and 2014 fiscal year-end exchange rates.

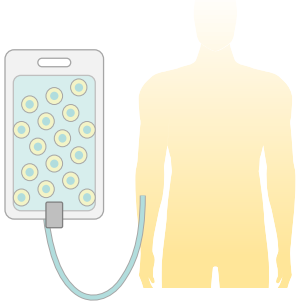
Mechanism of HLCM051 treatment

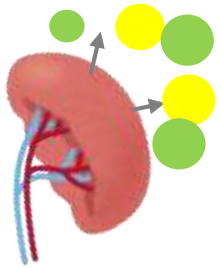
- Following intravenous administration after acute neurological injury, HLCM051 distributes to spleen, downregulating hyperinflammatory response.
- HLCM051 promotes the neuroprotective effect by releasing various cytokines and growth factors.



Stroke-induced neuronal damage (Primary)

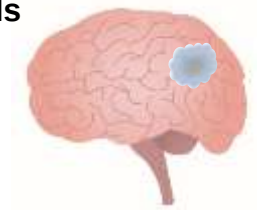
With HLCM051



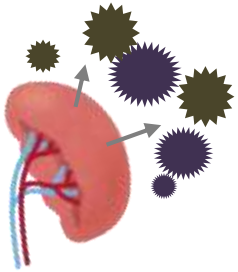


HLCM051
- **Suppress the mobilization/ release of inflammatory cells (lymphocytes, cytokines)**
- **Activate the mobilization/ release of anti-inflammatory cells**

Attenuate neuronal damage in the acute phase of stroke caused by inflammatory cells



Without HLCM051



Mobilization / release of inflammatory cells (lymphocytes, cytokines) in the spleen is activated

Exacerbate neuronal damage caused by inflammatory chemokines/ cytokines (Secondary)

Inflammatory cells are released from the spleen and exacerbate the neuronal damage of the ischemic site.

HLCM051 Clinical trial

Somatic stem cell regenerative medicine

HLCM051
MultiStem®

“Placebo-Controlled, Double-Blind, Phase 2/3 Efficacy and Safety Trial of HLCM051 (MultiStem®) in Patients With Ischemic Stroke”

Study Design

Subjects: Patients with onset of ischemic stroke within 18 to 36 hours prior to the start of the administration of the investigational product

Enrollment: 220 (HLCM051 group [n=110], or placebo group[n=110], randomized)

Number of Clinical trial sites: Plan to conduct at over 30 sites

Primary Endpoint: Proportion of subjects with an excellent outcome defined by the functional assessments on Day 90.

*Excellent Outcome

“Excellent Outcome” is defined as achieving mRs ≤1, NIHSS ≤1, and BI ≥95 in mRS, NIHSS, and BI, the three major indices of functional assessments for stroke patients.

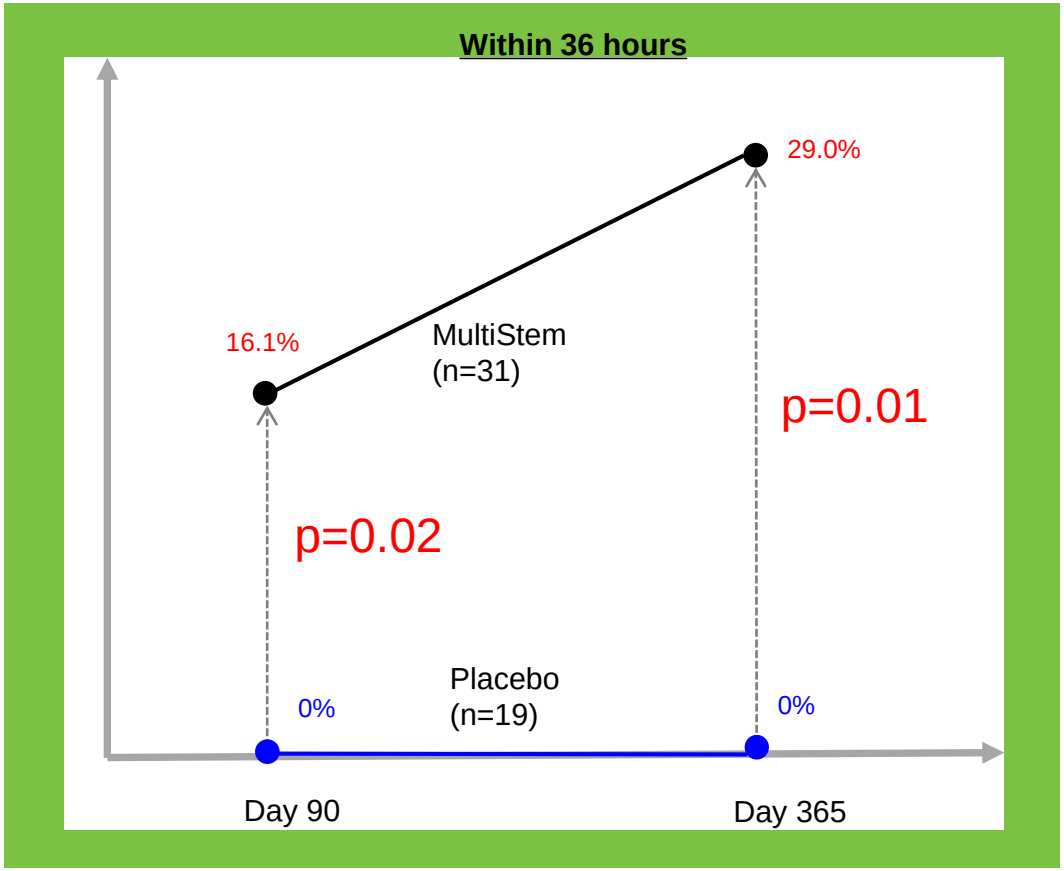
(Source) Image: prepared by Healios based on the materials provided by Athersys

Study Design Based on the Result of the Phase II Study by Athersys in Europe and America

Somatic stem cell regenerative medicine

HLCM051
MultiStem®

The proportion of patients who achieved Excellent Outcome was statistically significant (compared with the placebo group) both at Day 90 and Day 365 in the group of patients who had received MultiStem within 36 hours of the onset of cerebral infarction.



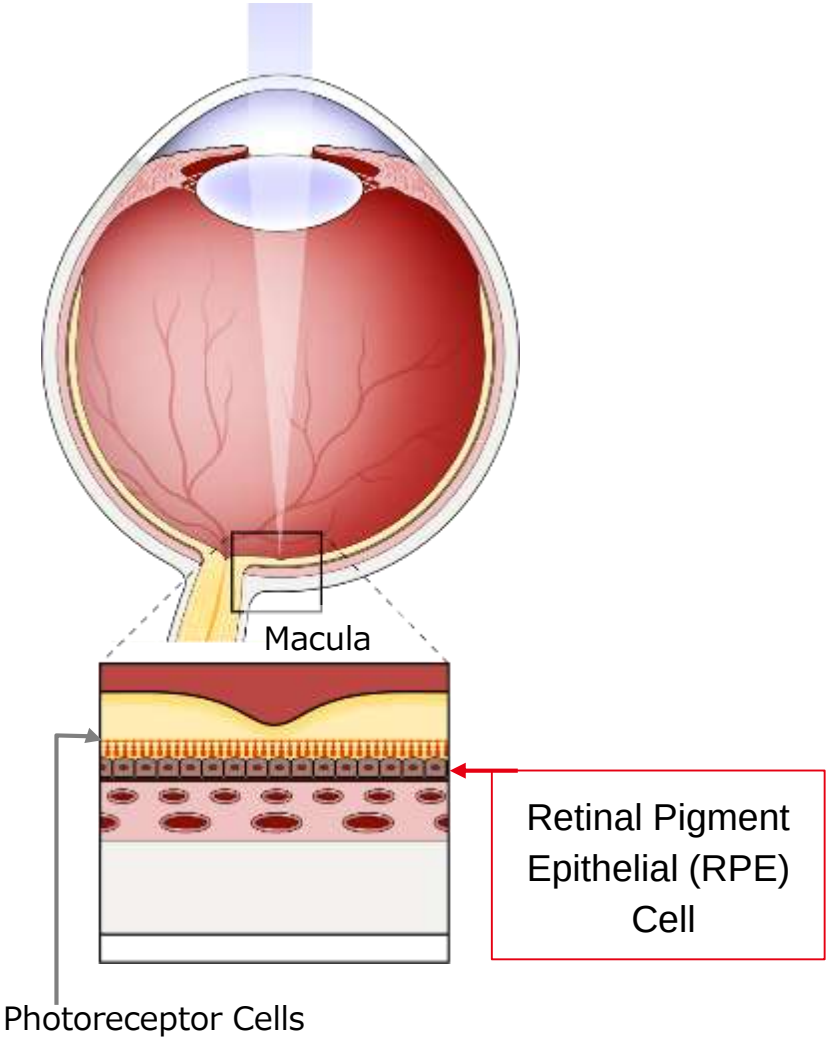
(Source) Prepared by Healios based on the data provided by Athersys.

(Note) Excellent outcome = All of the following: mRS ≤ 1, NIHSS ≤ 1, and BI ≥ 95)

4. Details of iPSC Regenerative Medicine

Explanation of AMD pathological condition

AMD causes RPE Cells to degenerate, which will damage functions



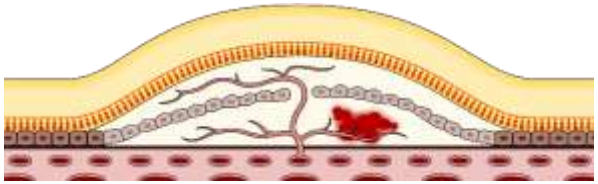
Regular Macular Part

Developed Dry AMD

Immunity Barrier Maintained
→ Degeneration of photoreceptor→ Dry AMD

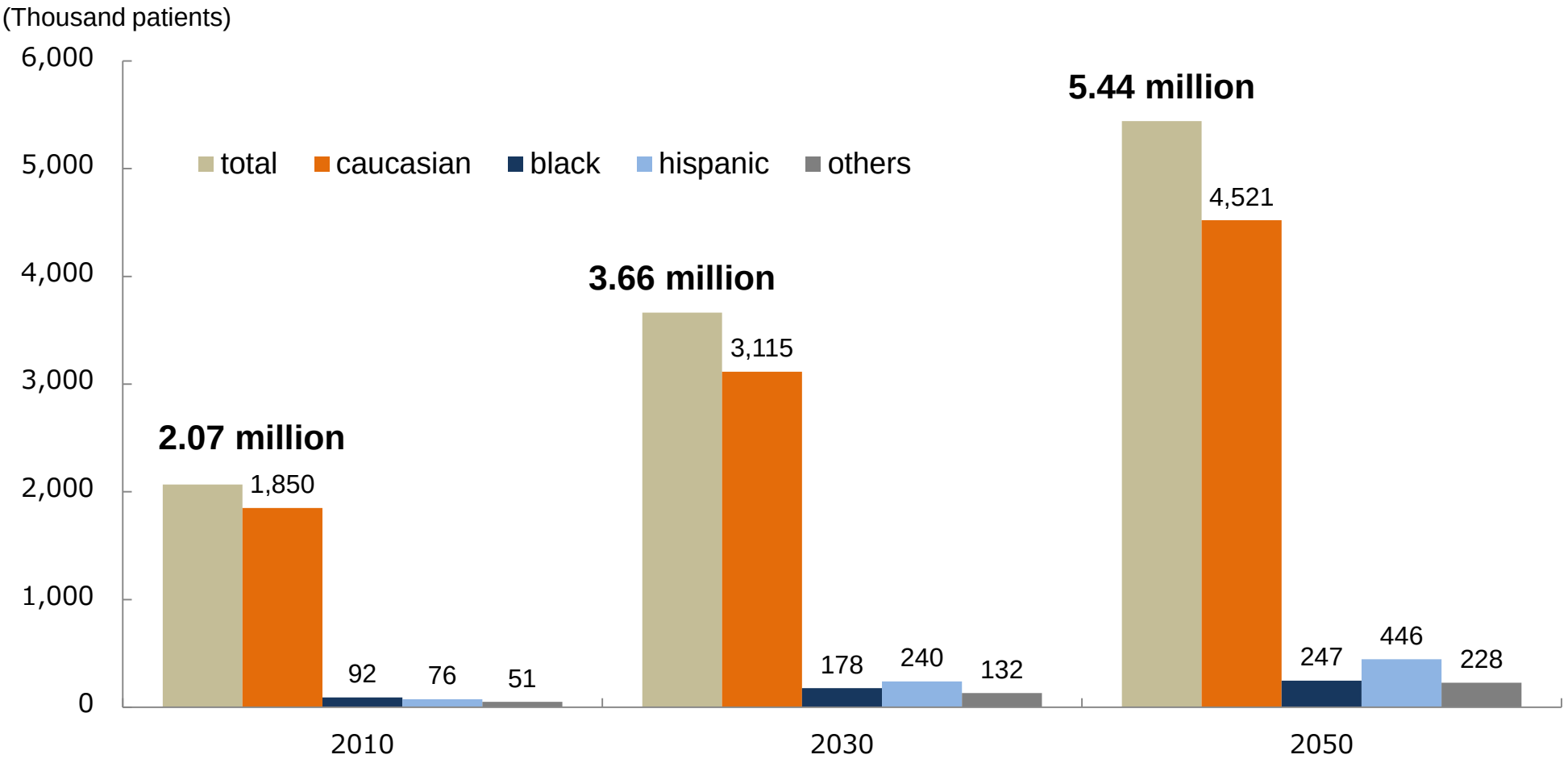
Wet AMD

Destruction of Immunity Barrier → Invasion of Immune Cells
→ Inflammation → Wet AMD



Estimated number of AMD future patients in serious cases in US

Expected to increase over medium- to long-term as society ages



(source) National Eye Institute

Number of AMD patients

Number of both Wet and Dry patients (including mild cases)

（Thousand patients）

	America	Japan	Others
Number of AMD Patients	**10,000**	**9,230**	**13,000**
Number of AMD Patients in Serious Cases	**2,000**	**690**	**2,600-3,220**
Wet-patients in serious cases	**1,000-1,500**	**630**	**1,300-1,950**
Dry-patients in serious cases	**850-900**	**60**	**1,100-1,170**

※According to research by Hisayama Kyushu University Graduate School of Medicine in Fukuoka (based on a comprehensive study), the total number of patients in Japan is calculated, estimating the total number of first-stage age-related macular degeneration and latter stage of age-related macular degeneration based on population statistics (2007). Also, the Disease Information Center announced that the number of patients suffering serious cases is approximately 690,000. The total number of patients in the US, which the National Eye Institute reports, includes the total number of age-related macular degeneration patients in mild cases and patients with visual field defects. Also, our company calculated the total number of Dry/Wet patients based on the incidence rates presented by AMDF (2010). Our company calculated the total number of patients in Europe based on incidence rates in each grade of European population statistics （2010)

※source: Prevalence of age-related maculopathy in older Europeans: the European Eye Study (EUREYE).Source: Arch Ophthalmol. 2006 Apr;124(4):529-35

Market scale of AMD

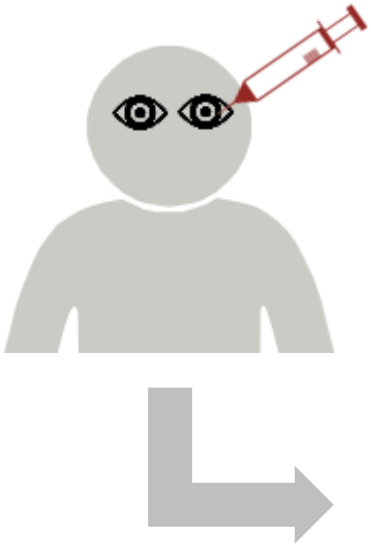
Annual sales of medicinal treatments of Wet AMD: 8.44billion USD.
No medicine for Dry AMD.

Condition	Medicine / Effect	Year	America	Japan	Others	Total
Wet	Anti-VEGF Medicine/ Restraint of New Blood Vessels	2016	**4,729 million USD**	**580 million USD**	**3,127 million USD**	**8,436 million USD**
Dry			**No Medicine**			

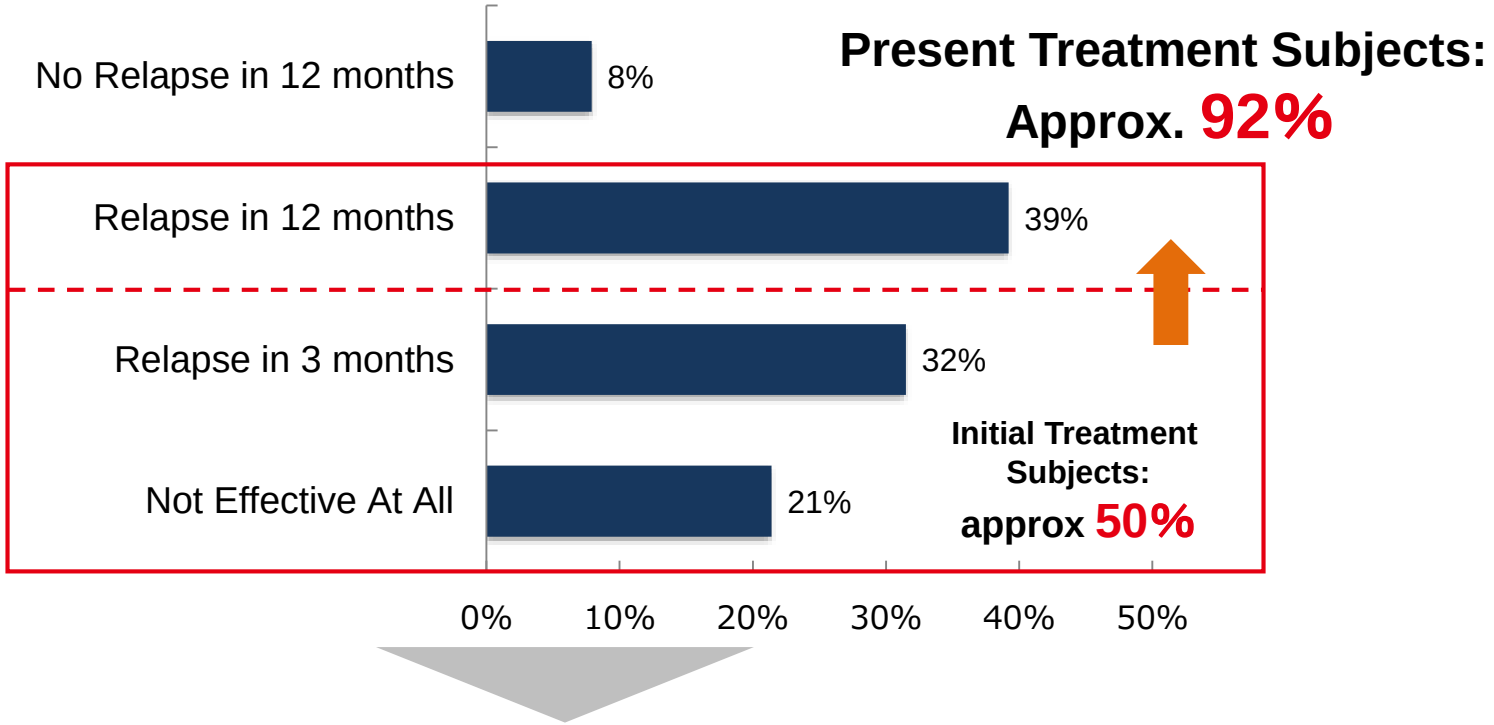
(source) Market scale was calculated using official materials from drug companies (Roche Diagnostic, Novartis, Regeneron, Bayer HealthCare, Santen Pharmaceutical Co., Ltd). Calculated using 2016 fiscal year-average exchange rates.

Treatment subjects for Wet AMD

Patients recurring within 1 Year, which is the case of approx. 92% of Wet AMD Patients, are the candidates for treatment.



Recurrence frequency after receiving anti-VEGF medication



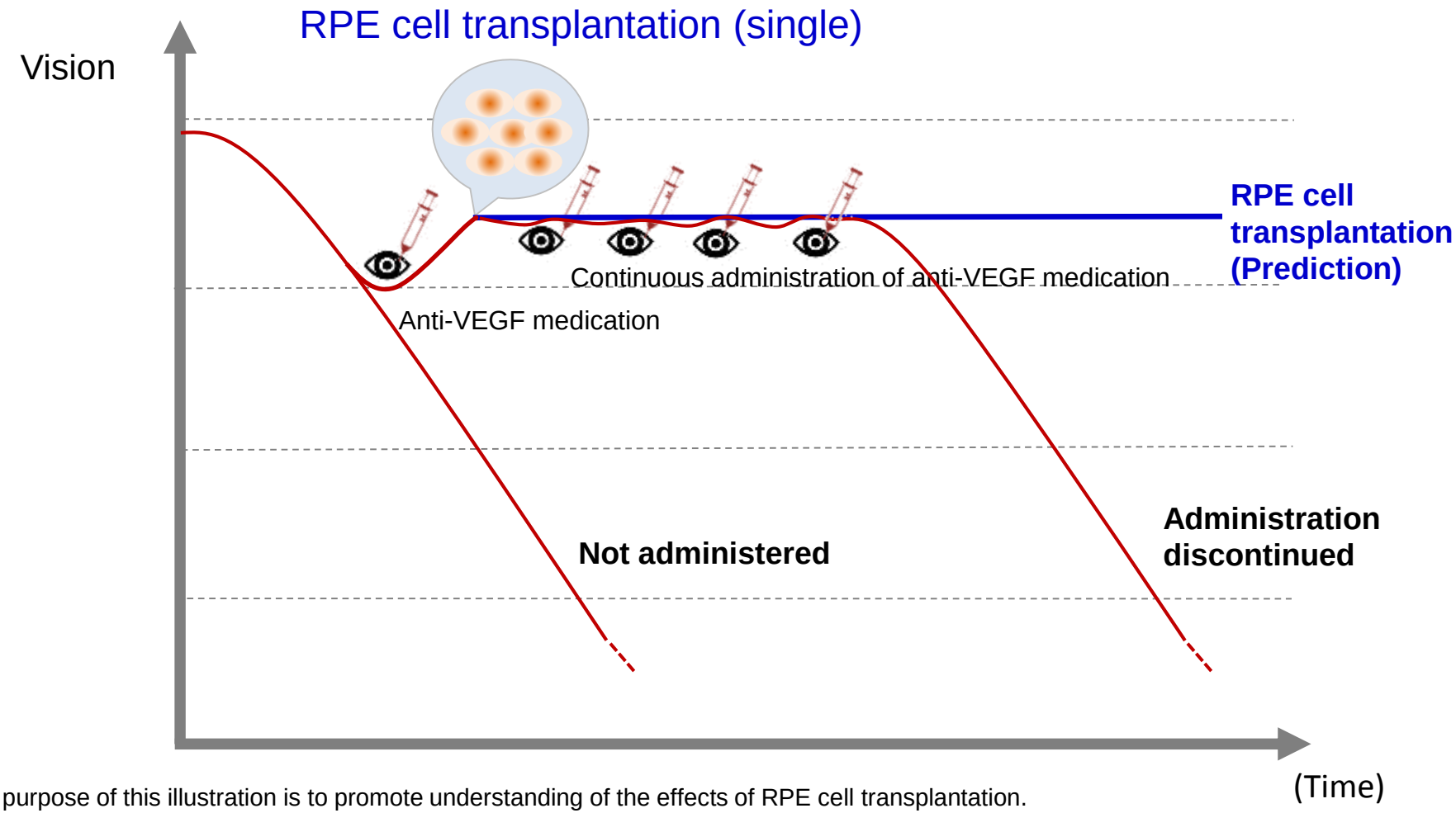
Present Treatment Subjects:
Approx. 92%

Initial Treatment Subjects:
approx 50%

QOL of continuously medicated patients is not high.

(source) 13th Annual Meeting of The Japanese Society for Regenerative Medicine March 19th 2014, Thurs, 12:00～12:50
Approach to Clinical Application of iPS cells Institute of Physical and Chemical Research, Mandai Michiko

Good vision can be maintained with early treatment



* The purpose of this illustration is to promote understanding of the effects of RPE cell transplantation.
Changes in vision with the administration of anti-VEGF medication vary according to patient symptoms and administration frequency.

Guide to medicine price – Approach from medical expense of existing health care

Anti-VEGF medicine mostly continues from the beginning of treatment until death

Annual Medical Expense

Unit Price of Anti-VEGF
170,000 yen

✖

Annual Recommended Medication Protocol
6 Times

=

Annual Medical Expense
1,020,000 yen

Estimate of Lifetime Medical Expense

On the Assumption of Average Life Span (Japan): 80years old (Male) / 86 years old (female)

Estimate of Lifetime Medical Expense

Continuous Treatment for **50-year old Patient Onset** ＝approx. **30years** ✖ **1.02 million yen** = **Approx. 30 million yen**

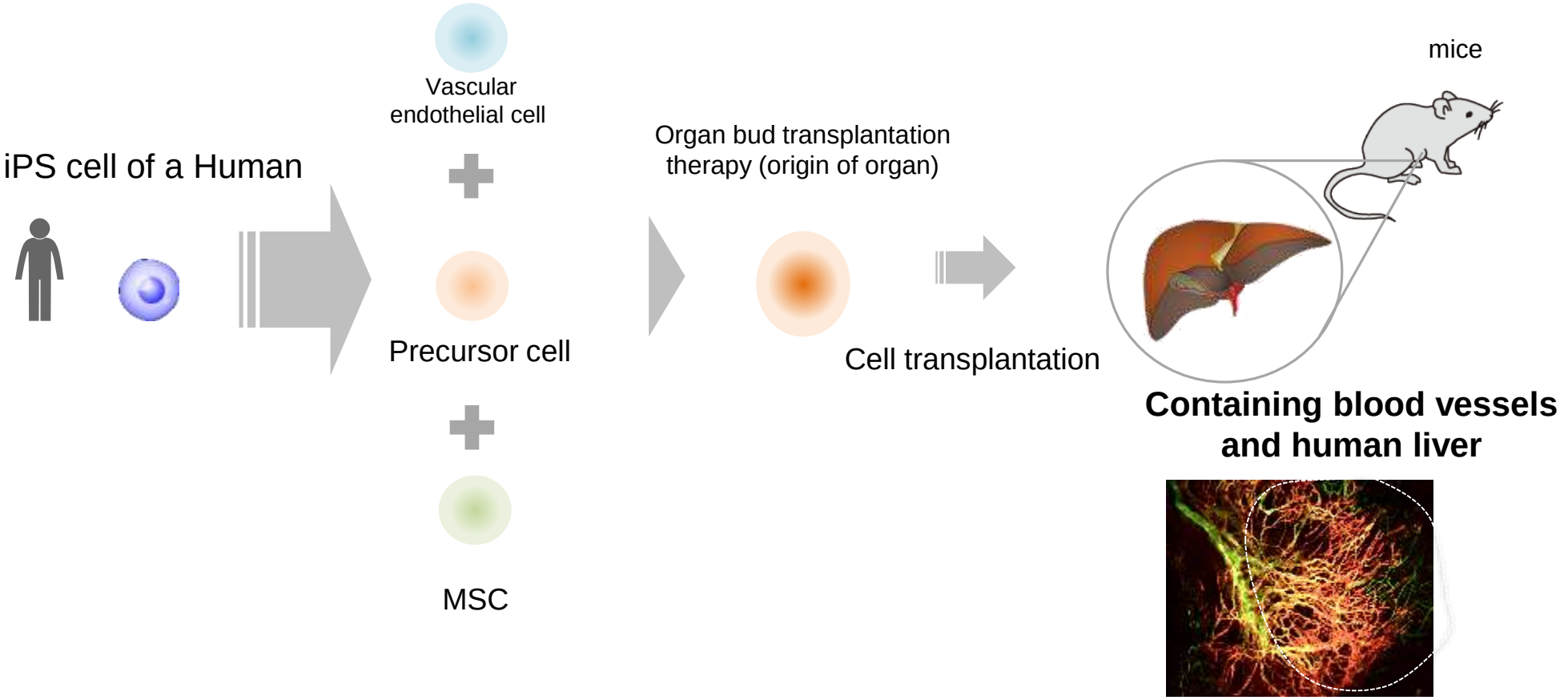
60-year old Patient Onset＝approx. **20years** ✖ **1.02 million yen** = **Approx. 20 million yen**

(source) Onset Data: National Eye Institute; Average Life Span: The Ministry of Health, Labor and Welfare; Annual Recommended Medication Protocol: Materials Presented by Institute of Physical and Chemical Research

5. Expansion to 3D Organs (Liver)

3D organ generation mechanism

Generating “Organ bud” by co-culturing 3 types of cells

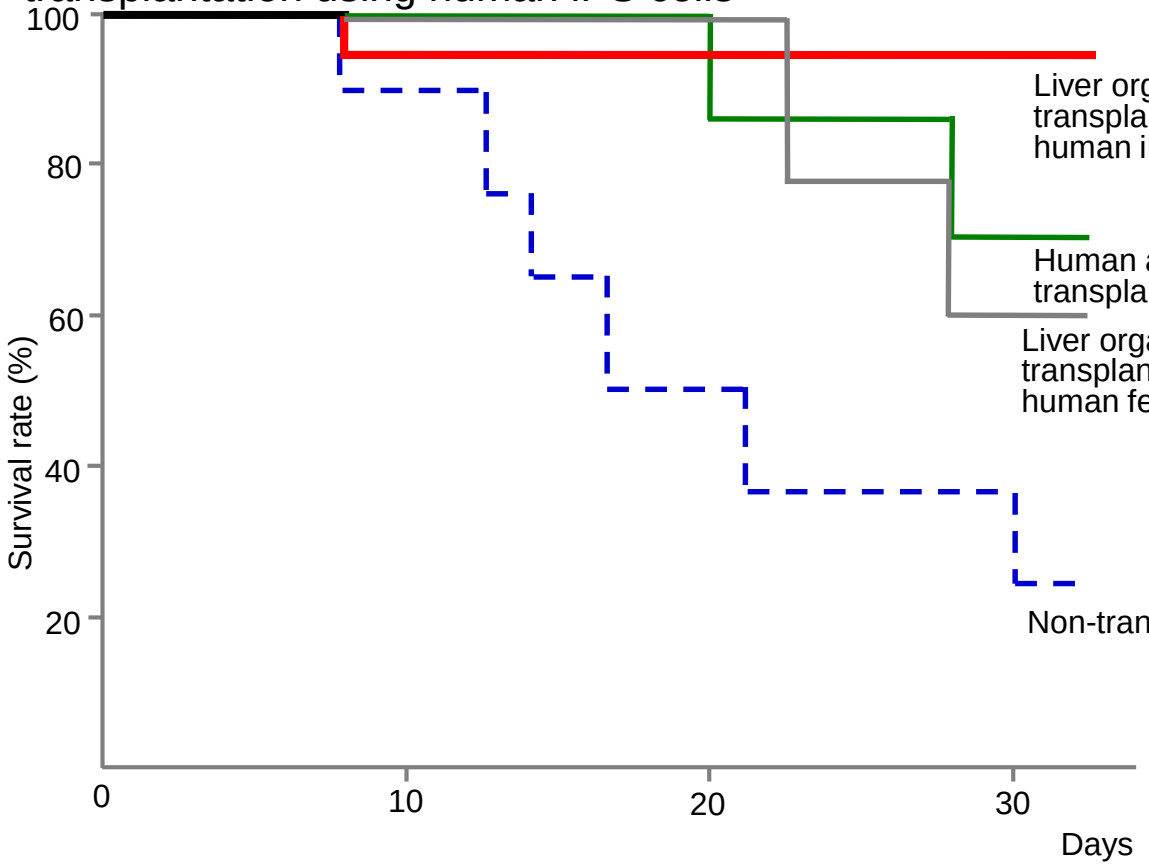


（Source）Takebe,T., et al. Nature Protocols, 9, 396–409 (2014)

Survival rate of liver failure model mouse

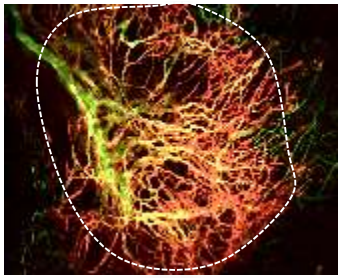
Survival rate improves significantly in transplantation experiments

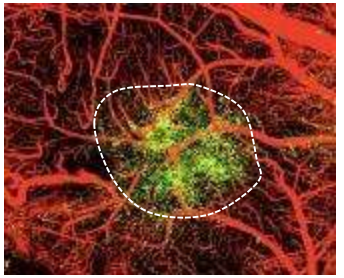
Treatment effects of liver organ bud transplantation using human iPS cells



(Source) Adapted by Healios from Takebe. T, et al. Nature, 499 (7459),（2013)

Process in which organ formed from organ bud links mouse ‘s vascular network autonomously





(Source) Takebe,T., et al.
Nature Protocols, 9, 396–409 (2014)

Metabolic liver disease in newborns

Yokohama City University planning to start clinical study in 2019

Urea cycle defect

Disease caused by congenital abnormality of enzyme functioning in metabolic pathway (urea cycle), which detoxifies ammonia in the liver and produces urea. Presently, the only definitive treatment available is liver transplantation.

* Even patients with minor conditions require treatment combining food treatment and medication to lower ammonia levels throughout their lives.

Estimated market size of metabolic liver disease in newborns

	US	Japan	Europe	Total
Number of patients (yearly)	**Approx. 160**	**Approx. 30**	**Approx. 230**	**Approx. 420**
Treatment costs (annual) Enzyme replacement therapy	**30 million yen – 50 million yen**			
Estimated annual market scale	**5 - 8 billion yen**	**1 - 1.5 billion yen**	**6 - 11.5 billion yen**	**12 - 21 billion yen**

∗ Number of patients and market size are estimated by Healios based on number of newborns and incidence rate.

6. Company Overview

Healios Overview

About Us

Company Name	HEALIOS K.K.（TSE: 4593）
Representative	Hardy TS Kagimoto, MD　President and CEO
Head Office	World Trade Center Building 15F 2-4-1 Hamamatsucho Minato-ku, Tokyo　Japan 105-6115
Paid in Capital	9,616 million yen (As of end of September, 2017)
Research Institution	Kobe and Yokohama
Number of Employees	71　(As of end of September, 2017)
Affiliated Company	SighRegen Co., Ltd. (Joint Venture with Sumitomo Dainippon Pharma Co., Ltd.)

Our Experienced Team

President and CEO
Hardy TS　Kagimoto, MD

- Succeeded in Developing BBG and Realized Sales in Europe

Director of Overseas Development
Al Reaves, Ph.D

- Responsible for innovative clinical programs for wet & dry AMD - Lucentis (X-US); Visudyne (global)

Director of Laboratories in Kobe, Research and Manufacturing
Kouichi Tamura, Ph.D

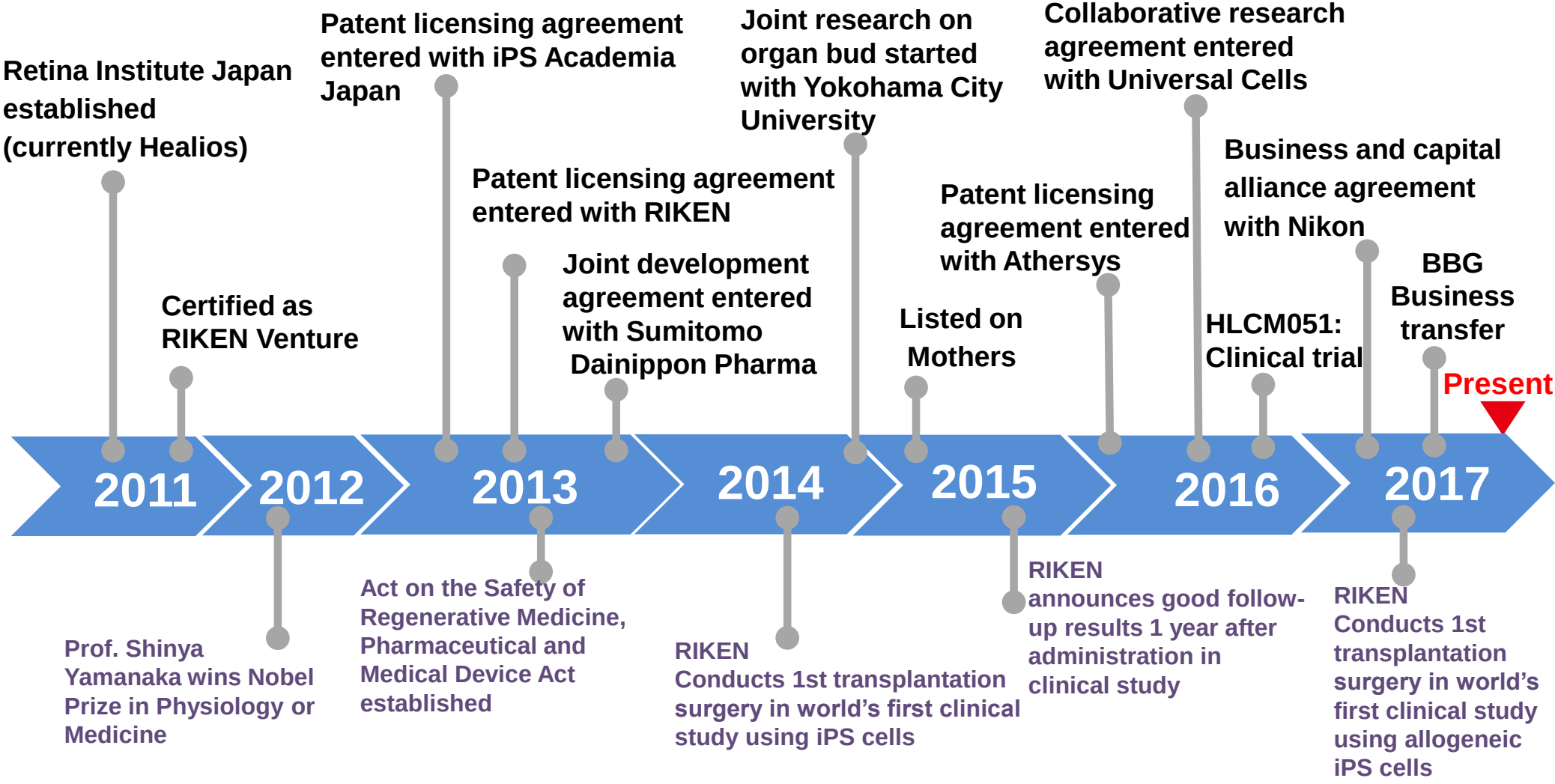
- Astellas US Director of Laboratories
- Well-acquainted with Immunosuppressant Research

Director of Domestic Development
Michihisa Nishiyama

- Constructed network for Tacrolimus approval and sales at Astellas in the US and Europe

Company History and Social Trends

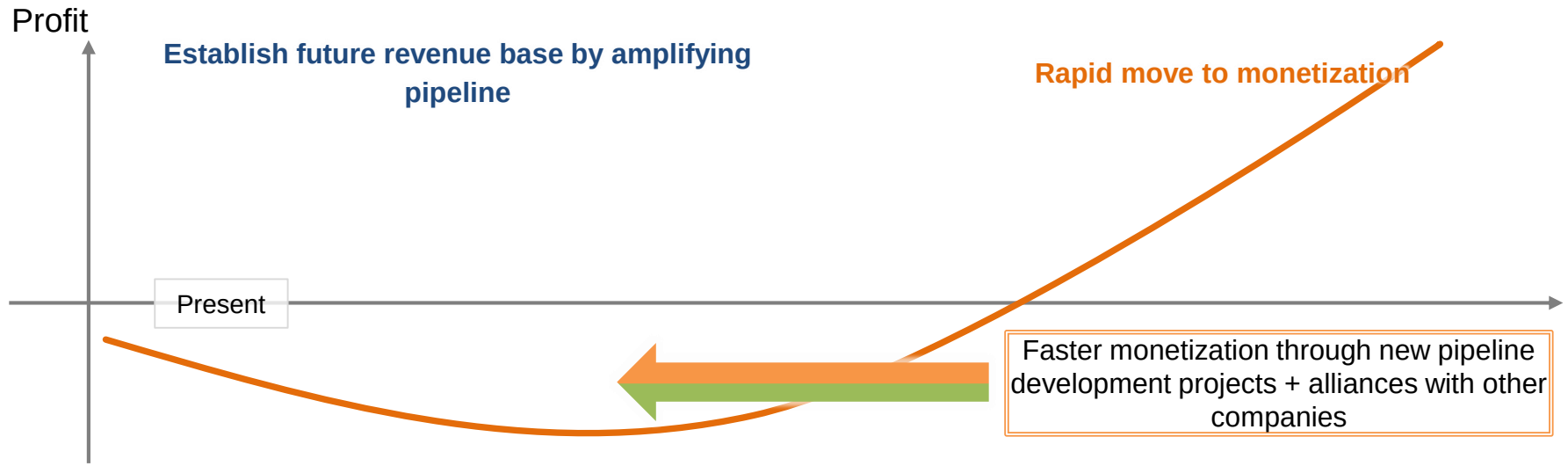
Pioneer of iPSC regenerative medicine development



Status of existing pipelines

Indications	Stage	Outline	Development funds
Wet AMD	Pre clinical	• About 600,000 patient subjects in Japan • Differentiation and transplant RPE cells from iPSC (aim is to outgrow symptomatic treatment using anti-VEGF medication) • In joint development with DSP	Financing based on joint development with DSP. (Milestone and development fee: total 6.8 bil Yen). Fundraising completed with 2015 listing.
Dry AMD	Pre clinical	• About 5 million patient subjects all over the world • Treatment of transplantation using iPSC derived RPE cells • No effective medication • Selection of development partner in process	Plan to prepare subsequent development costs through alliances, etc.
Metabolic Liver Disease	Pre clinical	• About 30 patient subjects in Japan; over 400 in the world • Mini-liver transplant for patients with congenital abnormalities in specific liver enzymes • Existing treatments cost more than ¥30 million / year • Yokohama City University plans to start clinical research in FY2019	Partial research costs already raised. Plan to prepare subsequent development costs through alliances, etc.
Ischemic Stroke	Clinical stage	• About 60,000 patient subjects in Japan • Cellular medication that improves post-stroke prognosis by suppressing immunoreaction • Hopes are for efficacy during 18-36 hours post-stroke, when there is no existing medication • In Phase 2/3 clinical trials. Testing assumed to take place for about two years	License fees and partial development funding already raised through loans. Next milestone is slated payment of about US$30 million.
ILM Peeling, etc. (BBG)	Business transfer	• April 2017, transferred the business to DWTI • Received a lump sum fee of 1.3 billion yen. There is also the possibility of receiving milestone payments.	-

Development & revenue planning



Wet AMD（Japan）	Pre clinical	Clinical trial	Application	
Dry AMD（Abroad）	Pre clinical			Application
Metabolic hepatic syndrome(Japan)	Pre clinical	Clinical research		Application
Ischemic stroke（Japan）	2016/9 Clinical trial	Completion of trial	Application	
New pipeline			Application	
New pipeline			Application	
Universal Cells Pipeline				Application

7. Circumstance of Regenerative Medicine

Rapid impact of modified regulations

Approval of regenerative medicine products, September 2015

Product Name	Temcell® HS Injection	Heart Sheet
Company	JCR Pharmaceuticals	Terumo
Indications	Acute GVHD after hematopoietic stem cell transplantation	Severe heart failure due to ischemic heart disease
Price	13.9 million yen	14.76 million yen
Important Point	First allogeneic cell-based regenerative product	First conditional approval

(note) Calculated using 2013 and 2014 fiscal year-end exchange rates.

Price calculation method prospects

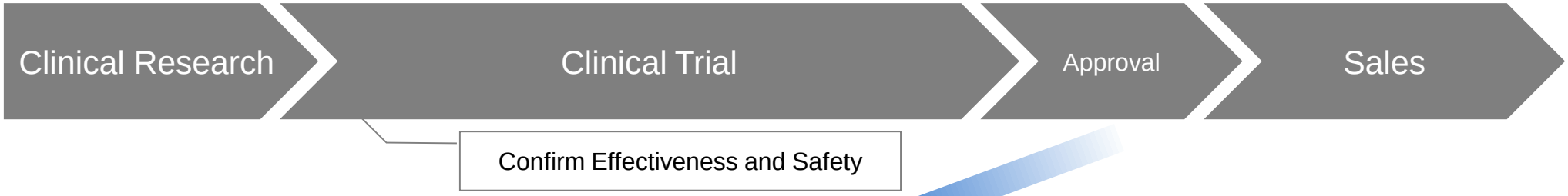
Cost accounting system

* The price of new drugs is basically calculated according to the prices of official articles with similar efficacy (price determination by comparable drug). However, if there are no appropriate similar official articles, required costs are added in the calculation of prices (cost accounting system).

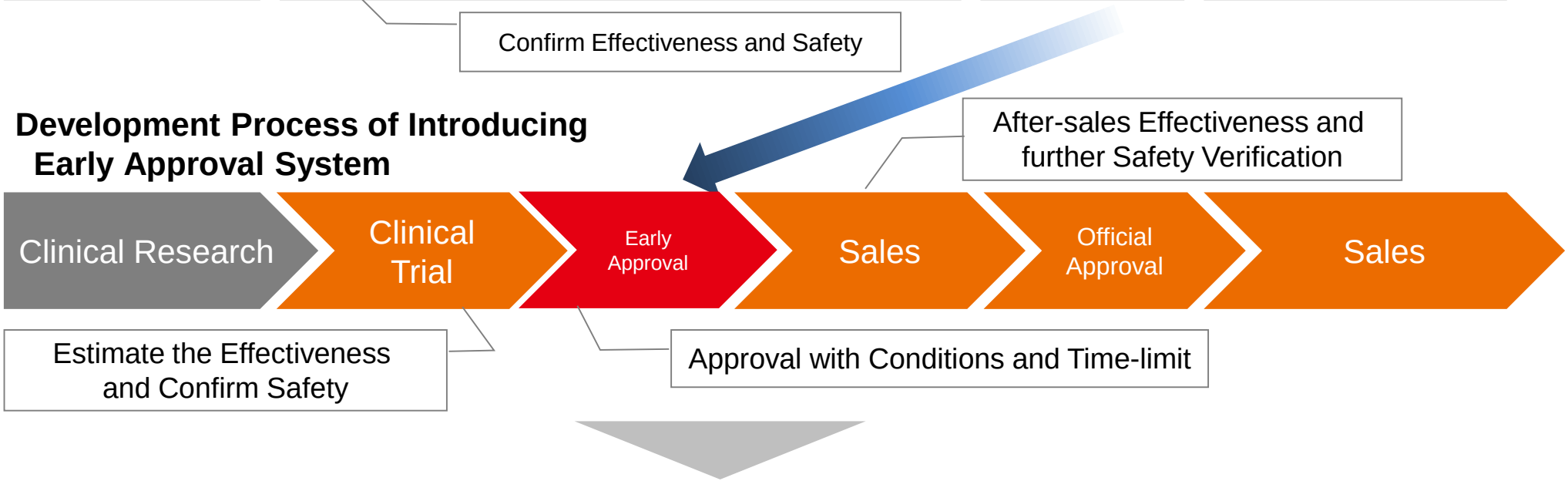
Historical Alleviation of Regulations

Japanese Government Revises Regulations to Put Japan at the Forefront

Process of the Development So Far



Development Process of Introducing Early Approval System



- Drastic reduction in the treatment period and number of patients with ‘Early Approval System’ .
- Insurance is listed at ‘Early Approval’ stage

Descriptions of future events, etc. in this document include Healios' assumptions, prospects, etc. based on information which could be acquired at the time this document was presented. For this reason, actual performance, development progress, etc. may differ from those described in this document according to the outcome of R&D in the future, the actions of regulatory authorities, etc. in the future, and uncertain/pending factors as of this point.

Also, this document contains information on regenerative medicine and medical equipment that are currently under development or already on the market. Such information is not intended for promoting advertising or providing medical advice.

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